Vancomycin-Resistant Enterococci Infections in the Department of Defense: Annual Report 2014

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Vancomycin-resistant Enterococci (VRE) are Gram-positive cocci that are resistant to vancomycin and most commonly infect seriously ill patients that have prolonged hospital stays or antibiotic use. Hospital acquired VRE infections are associated with high rates of morbidity and mortality and are a concern for hospitals around the world. The objective of this annual retrospective report is to summarize the VRE infection burden in the Department of Defense (DOD) and the Department of the Navy (DON) for calendar year (CY) 2014. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and healthcare-associated (HA) infection metrics for all DOD and DON beneficiaries. Overall, the incidence rates of VRE infections in the general United States (US) and DOD are decreasing while increasing for the DON populations. VRE risk groups did not substantially change in 2014 as VRE continues to predominately affect elderly females and manifest as urinary tract infections (UTIs). In addition, antibiotic susceptibility patterns did not substantially change in 2014. Daptomycin, linezolid and gentamicin remain viable treatments for VRE. HA infections have decreased in the last year but the overall exposure burden of VRE remains a major problem in the hospital setting. Improved infection control practices would help to minimize the spread of these infections.

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Abstract

Vancomycin-resistant *Enterococci* (VRE) are Gram-positive cocci that are resistant to vancomycin and most commonly infect seriously ill patients that have prolonged hospital stays or antibiotic use. Hospital acquired VRE infections are associated with high rates of morbidity and mortality and are a concern for hospitals around the world. The objective of this annual retrospective report is to summarize the VRE infection burden in the Department of Defense (DOD) and the Department of the Navy (DON) for calendar year (CY) 2014. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and healthcare-associated (HA) infection metrics for all DOD and DON beneficiaries. Overall, the incidence rates of VRE infections in the general United States (US) and DOD are decreasing while increasing for the DON populations. VRE risk groups did not substantially change in 2014 as VRE continues to predominately affect elderly females and manifest as urinary tract infections (UTIs). In addition, antibiotic susceptibility patterns did not substantially change in 2014. Daptomycin, linezolid and gentamicin remain viable treatments for VRE. HA infections have decreased in the last year but the overall exposure burden of VRE remains a major problem in the hospital setting. Improved infection control practices would help to minimize the spread of these infections.

Table of Contents

List of Tables and Figures

Executive Summary

The EpiData Center Department (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducts routine surveillance of clinically significant outcomes. This report provides a summary of the VRE infection burden in the DON and DOD for calendar year 2014.

Positive *Enterococcus* isolates were identified utilizing the Composite Healthcare System (CHCS) Health Level 7 (HL7) formatted microbiology data. Current rates of VRE infections were compared to previous years and the historic mean rate of infection among the DON and DOD. VRE infection rates were also compared by demographic and clinical characteristics to determine at-risk populations.

Overall, the incidence rates of VRE infections in the general US, DOD, and DON populations decreased. VRE risk groups did not substantially change in 2014 as the infection continues to predominately affect elderly females and manifest as UTIs. In addition, antibiotic susceptibility patterns did not substantially change in 2014. Linezolid, gentamicin, and daptomycin remain viable treatments for VRE.

Although this report indicates that current infection control practices seem to be decreasing healthcare-associated infections, VRE infections in hospitals are still a major threat for transmission of VRE in the DOD and the DON. Introduction of better infection control practices should help control healthcare associated infections.

Introduction

Enterococci are Gram-positive cocci that are normal inhabitants of the human gut, and typically do not cause infection unless the host has a suppressed or compromised immune system.[1] *Enterococcus* infections commonly manifest as UTIs, intra-abdominal cavity infections, and blood stream infections (BSIs).[2-4] A VRE species is any member of the *Enterococcus* genus that is resistant to vancomycin, a glycopeptide antibiotic.[1] *Enterococcus faecium* and *E. faecalis* are the species most commonly associated with VRE infections, though studies have identified *E. raffinosus* as the species with highest rates of resistance.[5,6] Experts hypothesize that resistance genes developed due to selective pressure caused by a drastic increase in the use of vancomycin during the 1980s and 1990s. This increased use was in response to another multi-drug resistant organism (MDRO), methicillin-resistant *Staphylococcus aureus* (MRSA), as well as the common use of prophylactic vancomycin for surgical and indwelling catheter patients.[7] Research identified varying resistance patterns among VRE strains caused by resistant genes passed between organisms.

VRE initially emerged in 1987 in Europe. Within a decade of identification, it spread and became a pathogen of concern in US hospitals, exhibiting resistance to multiple antibiotics and causing a wide range of infections with high mortality.[2] Mortality rates in patients with VRE bacteremia may reach up to 70.0%.[8] In 1992, 4.4% of US *Enterococcus* isolates were resistant to vancomycin, and the rate of nosocomial spread of VRE increased from 0.3% in 1989 to 7.9% in 1993; by 1995, the healthcare community reported pockets of endemicity.[1,2,9] By 1997, VRE was the second most common HA infection, linked to approximately 12.0% of all HA infections, and by 1999, VRE was associated with 17.0% of all HA infectionss.[10] After 1999, the rate of VRE incidence began to decrease, most likely as a result of the implementation of recommended infection control techniques from the Hospital Infection Control Practices Advisory Committee (HICPAC).[1]

However, current trends demonstrate that VRE infections are rising once again. One US study reported hospitalizations due to VRE infections increased from 3.2 per 10,000 hospitalizations to 6.5 per 10,000 total hospitalizations from 2003-2006.[11] Some European countries have also documented increasing rates of VRE infections, with vancomycin resistance reportedly as high as 28.0% among *E. faecium* isolates.[12] Experts believe that the widespread use of vancomycin to treat MRSA is an important reason behind the emergence, continued spread, and increasing trend of VRE infections in the US.[13]

There is a drastic difference between the virulence of European and US VRE strains. European VRE strains are frequently more benign and exist in a community reservoir; HA infections are not common.[3] Such a community reservoir does not exist in the US, where VRE HA infections have a higher rate of morbidity and mortality.[3] In the US, the major reservoir for VRE are hospitalized patients with gastrointestinal carriage of VRE.[8] Research supports the idea that VRE can be spread by direct person-to-person contact, including carriage on the hands of healthcare personnel, contaminated environmental surfaces, or patient care equipment.[8]

VRE infections tend to occur in seriously ill, hospitalized patients, especially among patients with prolonged hospital stays and patients who recently received organ transplants.[8] It is likely that vancomycin use predisposes patients to colonization and infection with VRE by inhibiting the growth of the normal Gram-positive intestinal flora and providing a selective advantage for VRE that may be present in small numbers in the individual's bowel.[8] Other risk factors for VRE infection include previous use of third generation cephalosporins, to which enterococci are intrinsically resistant; advanced age; severity of underlying condition; prior HA infection; pressure sores; and recent intra-abdominal surgery.[14-16]

HICPAC recommends prudent use of vancomycin, education of the hospital staff about VRE, effective use of the microbiology laboratory, and implementation of standard contact precaution protocols, such as isolation of infected patients and proper use of gloves and gowns, as ways to control transmission of VRE in hospitals.[8] Multiple studies show the positive impact that active surveillance of high-risk patients has on reducing the number of VRE infections in the healthcare setting.[17] One study in particular showed that active surveillance and contact precautions prevented VRE infections in an intensive care unit (ICU) in which 100% of the patients were colonized with VRE.[17]

Treatment for enterococcal infections normally includes an aminoglycoside plus another cell-wall active agent (β-lactam antibiotic). This is problematic for VRE infections, however, as they are often resistant to many, if not all, of these antibiotics, leaving few treatment options.[10] For patients allergic to penicillin or who have ampicillin- or penicillin-resistant strains, clinicians highly recommend vancomycin used in combination with other antibiotics, including aminoglycosides.[8] Quinupristin/dalfopristin was the first antibiotic developed for VRE. This antibiotic is only meant for treatment of *E. faecium*, as other *Enterococcus* isolates are intrinsically resistant to it. Since research identified that the use of quinupristin/dalfopristin was associated with debilitating adverse events, it has not been widely used since 2001.[18] Linezolid, an oxazolidinone developed in 2000, is another relatively new first line antibiotic and is effective against *E. faecium* and several other *Enterococcus* species. Some resistance has already been reported for linezolid.[18] Resistance has also been documented with daptomycin, which was developed in 2003 and is another treatment option for Gram-positive bacterial infections.[18] Fluoroquinolones are not highly recommended to treat VRE infections, as there are other classes of antibiotics that are more effective in clearing infection. However, fluoroquinolones are quite effective in the treatment of UTIs.[8]

The objective of this annual retrospective report is to summarize the VRE infection burden in the DOD and the DON for calendar year (CY) 2014. This summary includes demographic and clinical characteristics, antibiotic susceptibility patterns, prescription practices, and HAI metrics for all DOD and DON beneficiaries.

Methods

Positive cultures for *Enterococcus* were identified from microbiology data in Composite Heathcare System (CHCS) Health Level 7 (HL7) format that originated from fixed military treatment facilities (MTFs) including facilities outside the continental United States (OCONUS). Any *Enterococcus* species isolate resistant to vancomycin was considered a VRE isolate. BacLink and WHONET software programs, developed by the World Health Organization (WHO) to aid in the identification and analysis of MDROs, were used to identify VRE isolates and organize antibiotic susceptibilities within microbiology records.[19] VRE prevalence cases were defined as unique VRE isolates per person per 30 days. VRE incidence was defined as the first unique VRE isolate per person per calendar year. Surveillance cultures for VRE, which include all rectal swabs, were excluded from this analysis, as surveillance cultures are usually indicative of colonization and not true infection.

Demographics were described using variables within the HL7 microbiology records. The TRICARE region was defined by the region of the servicing MTF, identified by the requesting Defense Medical Information System (DMIS) identification number. Age was defined as patient age at the date of specimen collection using date of birth. Sponsor service (Air Force, Army, Marine Corps, and Navy only) and beneficiary status (Active Duty, Recruit, Retired, Family Member, and Other) were identified by the patient category code. The Family Member beneficiary category included family members of active duty service members and retirees; all other family members and beneficiaries (including National Guard members, reservists, and civilians) were given the beneficiary category designation of Other.

Clinical characteristics were also described using variables within the HL7 microbiology records. Encounter type was defined by the first letter of the four-letter Medical Expense and Performance Reporting System (MEPRS) code, with "A" indicating an inpatient encounter and all other codes grouped as outpatient encounters. Specimen sources and body site fields were used to categorize isolates into the following infection types: urinary tract, blood stream, gastrointestinal tract, skin and soft tissue, respiratory, sterile, and other. To classify surgical VRE infections, the HL7 microbiology records indicating a VRE infection were linked to the Standard Inpatient Data Record (SIDR) database using a unique identifier. The International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes found in the SIDR database were used to classify a specimen as surgical. Only intra-abdominal surgeries are a significant risk factor for a surgical site acquisition of VRE, therefore, only intra-abdominal procedures were considered in defining the surgery infection type.[15,16] Surgery was defined using the 2014 National Healthcare Safety Network's (NHSN) ICD-9-CM code listing of intra-abdominal surgeries.[20]

The antibiotic susceptibility test results from the microbiology records were used to create an antibiogram. The first VRE isolate per patient per year was included. The antibiotics included in the antibiogram were based on the Clinical and Laboratory Standards Institute (CLSI) testing guidelines for *Enterococcus* species isolates.[21] The Cochran-Armitage test was used to examine trend across the surveillance period.

Hospitalization records from the SIDR database were also used to examine VRE exposure and infection burden metrics within the MTFs. Infections were classified as hospital-onset (HO), healthcare-associated (HA), or community-onset (CO) VRE infections. A patient was considered to have an HO VRE infection if the specimen collection date was between the patient's admission and discharge dates and at least three days following the admission date. An infection was considered to be HA if an inpatient encounter occurred within the 12 months prior to the current specimen collection date, indicating recent exposure to the hospital environment. Other factors commonly used to define HA infections, such as the presence of an invasive device at the time of infection, patient history of surgery or dialysis, or residence in a long-term care facility, were not used to further define HA infections due to lack of data.[22] All outpatient encounters with a positive VRE culture were considered to be CO. Individuals who had a specimen collection date within three days from the admission date and no documentation of an inpatient encounter within the 12 months prior to the current specimen collection date were also considered to be CO.[22]

Seven HAI metrics were used in this analysis, including metrics for admissions prevalence, overall prevalence, HO bacteremia, HO UTIs, surgical site infections (SSIs), central line-associated bloodstream infections (CLABSIs), and ventilator-associated pneumonia (VAP). These were based on the National Healthcare Safety Network (NHSN) guidelines and HICPAC position paper on recommended metrics for MDROs.[22,23] The admissions prevalence metric measured the magnitude of VRE imported into fixed DOD MTFs, and the overall prevalence metric measured the magnitude of a patient's exposure in the healthcare setting to other patients with VRE. For the infection burden metrics, only the first HO VRE isolate per patient per admission was selected. Table 1 presents the classification for each metric.

Table 1. Classification of Infection Burden Metric Parameters

Metric	Definition
Overall prevalence	Any record where VRE was isolated from specimen collected at least three days after admission
Admissions prevalence	Any record where VRE was isolated from specimen collected within the first three days of admission
Hosptial onset bacteremia	Any record with body site or specimen source of blood that was collected at least three days after admission
Hospital onset urinary tract infections	Any record with body site or specimen source of urine that was collected at least three days after admission
Surgical site infections	Any record following NHSN operative procedure groupings[20]; The procedure is within admission and discharge dates; AND Infection occurs within 30 days of the procedure
Central line-associated bloodstream infections	Any record with body site or specimen source of blood; Records with ICD-9-CM procedure codes: 38.91, 38.92, 38.93, or 38.97; AND Specimen was collected at least three days after admission
Ventilator-associated pneumonia	Any record with body site or specimen source of respiratory sample; Records with ICD-9-CM procedure codes: 96.7, 96.04, 96.71, or 96.72; AND Specimen was collected at least three days after admission

Records are from linked Health Level 7 (HL7) microbiology data and the Standard Inpatient Data Record (SIDR).
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 4 February 2014.

Overall prevalence and admissions prevalence denominators were calculated using the total number of hospital admissions per year.[21] For the surveillance period, average rates were calculated and 95.0% confidence intervals (CIs) were calculated using an unpaired two-tailed Poisson distribution. Incidence density rates for HO bacteremia and HO UTIs were calculated as the total number of infections per the total number of patient-days per 100,000 patient-days. Patient-days were calculated as the sum of the lengths of stay for all admissions in a given year. Incidence density rates for device-associated infections (CLABSIs and VAP) were calculated as the total number of infections per 100,000 device-days. Device-days were estimated as the sum of the lengths of stay for all admissions that indicated the use of the device of interest (central line or ventilator) during the admission. SSI rates were determined by dividing the number of SSIs by the sum of all surgical procedures performed in 2013. Rates were only calculated if the total number of infections was greater than or equal to five.[22]

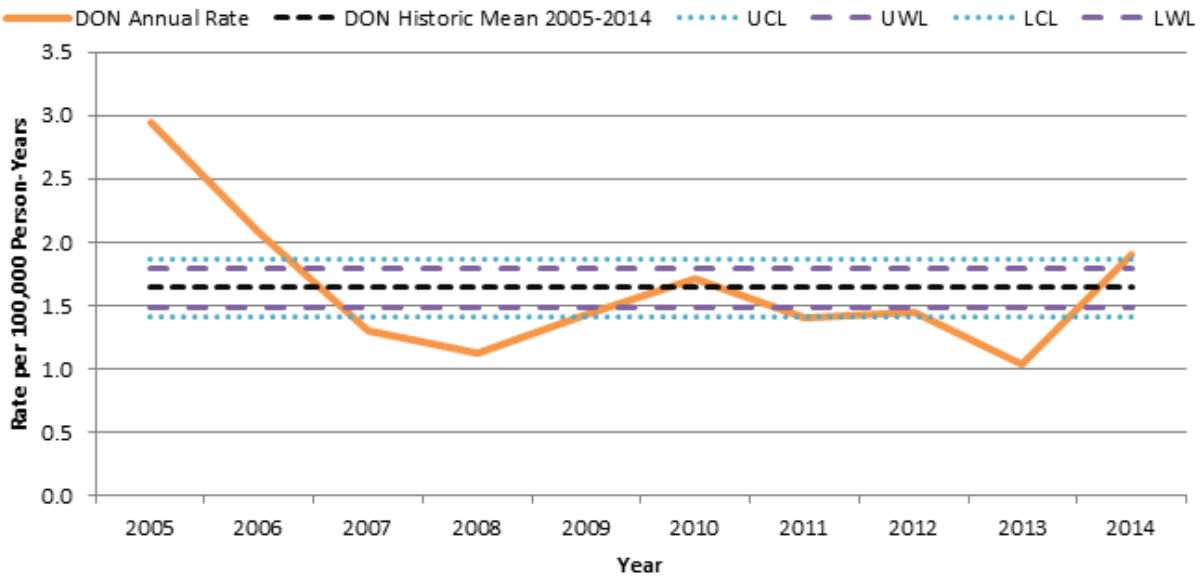
The statistical process control (SPC) was used to evaluate the statistical variation of VRE infection occurrences over the surveillance period. The mean incidence rates for the DOD and DON were calculated as the average infection rate from the nine-year period (2005-2013). The MHS Mart (M2) eligible beneficiary counts for the month of July of each year were used as a proxy for the average beneficiary count for that entire year. This proxy was also used as a denominator for calculating rates. Upper and lower warning limits (UWL, LWL) and upper and lower control limits (UCL, LCL) were calculated using two standard deviations above (UWL) or

below (LWL) the mean rate, and the UCL and LCL were calculated using three standard deviations above (UCL) or below (LCL) the mean rate.[24] Demographic rates were also calculated using the M2 July/yearly counts as the denominator. All rates are presented per 100,000 beneficiaries, unless otherwise specified.

Results

In CY 2014, the annual incidence rate of VRE infection for the DOD beneficiary population was 1.5 per 100,000 person-years. Overall, the VRE incidence rate decreased since 2005 but increased 29% from CY 2013 to CY 2014 and is now almost equal to the DOD historic mean rate. The incidence rate is no longer below the LCL. (Figure 1)

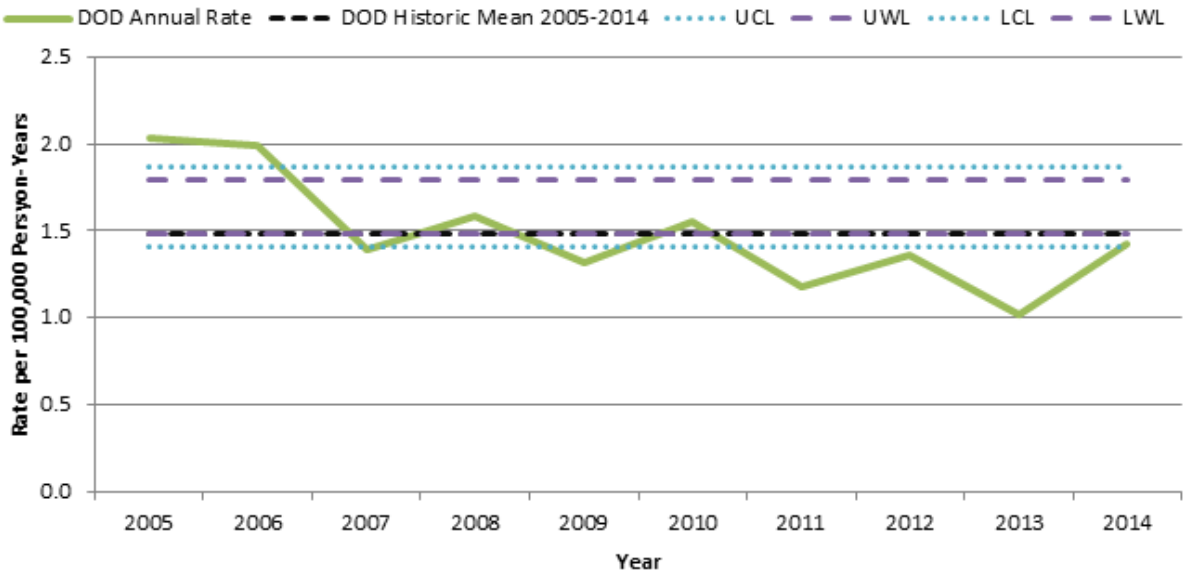
Figure 1. VRE Incidence Rates[a] among Department of Defense Beneficiaries, CY 2005-2014



[a] Incidence was identified as the first VRE isolate per person per year.
DON historic mean calculated from 2005 - 2013 as 1.6 cases per 100,000 person-years.
Data source: NMCPHC Health Level 7(HL7) formatted microbiology and MHS Mart (M2).
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 12 March 2015.

The DON annual incidence rate for VRE infection in CY 2014 was 1.6 per 100,000 person-years. There has been a decrease in VRE incidence in the DON since 2005, with the exception of a peak in 2010 and 2014. CY 2014 marks the most substantial increase in incidence rate (44%) over the nine year time frame. Similar to the DOD, the 2014 annual incidence rate is increasing, however, the DON incidence rate is now above the DON mean rate. The 2014 DON VRE incidence rate is also higher than the UCL.

Figure 2. VRE Indidence Rates[a] among Department of the Navy Beneficiaries, CY 2005-2014



[a] Incidence was identified as the first VRE isolate per person per year.
DOD historic mean calculated from 2005 - 2013 as 1.5 cases per 100,000 persons per year.
Data source: NMCPHC Health Level 7(HL7) formatted microbiology and MHS Mart (M2).
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 12 March 2015.

In CY 2014, there were 147 cases of VRE infection in the DOD. Of those, 54 (36.7%) were among DON beneficiaries (Table 2). For both the DOD and DON in CY 2014, higher rates of infections occurred among individuals aged 65 years or older, retired service members and in the West TRICARE region. This pattern also occurred for previous years, 2005 to 2013 (data not shown). In 2014, the highest rate of infection in the DOD sponsor services was among Navy beneficiaries at 2.3 per 100,000 eligible beneficiaries.

Table 2. Demographic Description of VRE Prevalent Cases among DOD and DON Beneficiaries, CY 2005-2014

	DOD		DON	
	2014 (N =147)		2014 (N = 54)	
	Count	Rate[a]	Count	Rate[a]
Gender				
Female	66	1.4	33	2.5
Male	71	1.5	21	1.4
Age Group				
0-17 years[b]	10	0.5	3	--
18-24 years[b]	3	--	3	--
25-34 years[b]	2	--	2	--
35-44 years[b]	5	0.6	3	--
45-64 years	36	1.8	16	2.6
65+ years	81	3.8	27	4.6
Sponsor Service				
Air Force	44	1.7		
Army	39	1.0		
Marine Corps	6	0.8	6	0.8
Navy	48	2.3	48	2.3
Beneficiary Type				
Active duty	6	0.4	5	1.0
Family member	71	1.4	33	2.1
Retired	58	2.8	16	2.6
Otherb	2	--	0	--
TRICARE Region				
Alaska[b]	0	--	0	--
North	43	1.5	21	2.0
OCONUS[b]	4	--	1	--
South[b]	33	1.1	4	--
West	57	2.1	28	3.1
Unknown[b,c]	0	--	0	--

[a]Rates calculated per 100,000 beneficiaries

[b]Rates are only presented if the count is higher than five.

[c]TRICARE service region cannot be determined from the microbiology data.

Data source: NMCPHC Health Level 7 (HL7) formatted microbiology .

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 12 March 2015.

Concerning clinical characteristics of the VRE infections within the DOD and DON in CY 2014, the majority of VRE infections identified were found in the inpatient setting for the DON and outpatient for the DOD, classified as CO, and diagnosed as UTIs (Table 3). For 2014, within the DOD, *E. faecium* caused 49.0% of VRE infections, while an unspecified *Enterococcus* species caused 50.9 % of infections in the DON. Only a small number of VRE infections were classified as HO VRE for the DOD and the DON, accounting for 7.4% and 12.3% of VRE infections, respectively (Table 3). HO VRE infections doubled since 2013, otherwise, findings from 2014 are similar to historical trends from 2005 to 2013 for both the DOD and DON (data not shown).

Table 3. Clinical Characteristics of VRE Prevalent Cases among DOD and DON Beneficiaries, CY 2005-2014

	DOD		DON	
	2014 (N =149)		2014 (N = 57)	
	Count	Percent	Count	Percent
Encounter Type				
Inpatient	68	45.6	30	52.6
Outpatient	69	46.3	24	42.1
Healthcare/Community Associated[a]				
Hospital onset	11	7.4	7	12.3
Healthcare associated	36	24.2	15	26.3
Community onset	46	30.9	18	31.6
Infection Type				
Urinary Tract	81	54.4	26	45.6
Blood Stream	15	10.1	6	10.5
Gastrointestinal Tract	3	2.0	1	1.8
Surgery	4	2.7	2	3.5
Skin and Soft Tissue	20	13.4	11	19.3
Respiratory	1	0.7	0	0.0
Sterile	2	1.3	1	1.8
Other	8	5.4	5	8.8
Species				
Enterococcus sp. unspec.	49	32.9	29	50.9
E. faecalis	17	11.4	4	7.0
E. faecium	51	34.2	15	26.3
E. gallinarum	9	6.0	1	1.8
E. casseliflavus	10	6.7	4	7.0
E. durans	0	--	0	--
E. raffinosus	1	0.7	1	1.8

[a]A VRE isolate can be classified as more than one healthcare or community associated exposure, therefore the counts may be greater than the total N.

Data source: NMCPHC Health Level 7 (HL7)microbiology and Standard Inpatient Data Record (SIDR).

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 12 March 2015.

Table 4 presents an antibiogram for the VRE isolates identified in the DOD from 2005 to 2014. There were a few instances where the numbers of isolates tested were less than 30, and those values should be considered with caution. VRE isolates among DOD beneficiaries in 2014 were most susceptible to daptomycin and least susceptible to ciprofloxacin. Overall, the susceptibilities for the antibiotics evaluated remained stable over the surveillance period. Ampicillin, gentamicin-high, penicillin, and streptomycin-high had significant ascending trends during the surveillance period (*P*-value <0.05), while tetracycline had a significant descending trend (*P*-value <0.0001). For the DON, the isolate counts were very low and would not support a meaningful antibiogram.

Table 4. Antibiogram of Vancomycin-Resistant *Enterococcus* species (VRE) Isolates Identified among the Department of Defense, CY 2005-2014

Antibiotics	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	*P*-value[b]
Ampicillin	15.7% 115	13.5% 104	15.9% 69	25.9% 81	25.3% 79	25.2% 119	23.8% 101	32.1% 109	35.4% 82	38.4% 99	<0.0001
Ciprofloxacin	11.9% 84	6.7% 60	15.4% 39	4.4% 45	7.5% 53	8.8% 68	10.8% 37	4.2% 48	17.1% 35	12.8% 47	0.9817
Daptomycin[c]	-- 0	100.0% 22	100.0% 10	100.0% 14	100.0% 13	100.0% 13	100.0% 10	100.0% 15	100.0% 16	89.4% 47	N/A
Doxycycline[c]	85.7% 42	92.0% 25	75.0% 16	66.7% 12	75.0% 16	50.0% 20	33.3% 12	25.0% 8	33.3% 6	46.2% 13	N/A
Erythromycin[c]	8.3% 12	0.0% 14	10.0% 10	7.7% 13	14.3% 14	16.7% 18	0.0% 11	0.0% 15	0.0% 5	0.0% 5	N/A
Gentamicin-High	68.8% 96	68.2% 85	66.7% 75	69.3% 88	70.3% 74	62.5% 80	64.7% 68	78.1% 73	87.1% 62	82.9% 82	0.0003
Levofloxacin[c]	29.2% 24	16.7% 48	30.4% 23	19.4% 31	8.3% 24	14.3% 35	11.8% 34	20.7% 29	25.0% 32	19.1% 47	N/A
Linezolid[c]	92.0% 75	90.4% 73	90.9% 33	91.3% 46	95.5% 44	85.5% 55	88.2% 34	88.6% 35	92.9% 28	86.7% 45	0.3592
Nitrofurantin	44.6% 56	58.5% 53	38.7% 31	46.2% 39	35.4% 48	33.9% 59	46.3% 41	44.2% 52	47.5% 40	56.4% 55	0.742
Penicillin	18.2% 43	15.3% 144	13.4% 82	21.0% 100	21.3% 89	20.8% 101	18.6% 70	21.4% 70	36.2% 58	30.1% 73	0.0009
Quinupristin/Dalfopristin[c]	76.1% 71	85.7% 70	82.4% 34	73.8% 42	84.2% 38	81.0% 42	72.0% 25	85.7% 28	75.0% 20	72.2% 18	N/A
Rifampin[c]	7.1% 56	16.7% 30	11.8% 17	25.0% 16	0.0% 21	14.8% 27	20.0% 15	14.3% 21	15.4% 13	20.0% 20	N/A
Streptomycin-High	41.1% 112	46.2% 93	62.9% 70	64.0% 86	64.9% 74	64.6% 82	66.7% 66	73.8% 65	81.5% 54	66.7% 72	<0.0001
Tetracycline	63.9% 97	61.2% 85	75.0% 48	58.1% 62	49.3% 69	35.3% 85	23.0% 61	22.4% 76	19.0% 58	20.8% 77	<0.0001

[a]Only the first vancomycin-resistant *Enterococcus* species isolate per patient per calendar year were included; surveillance cultures were excluded.

[b]*P*-values were determined using the Cochrane-Armitage test for trend.

[c]Treat with caution if isolate counts are less than 30.

Data source: NMCPHC Health Level 7 (HL7) formatted microbiology .

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 13 March 2015.

Table 5 displays the exposure burden for DOD and DON VRE HA infections. Both the admissions and overall prevalence rates for 2014 are lower than the calculated historic mean. The rate of VRE importation into fixed MTFs for 2014 was 19.1 per 100,000 admissions for the DOD and 16.0 per 100,000 admissions for the DON. The overall prevalence of VRE infections for the DOD and DON in 2014 were 24.8 per 100,000 admissions and 22.6 per 100,000 admissions, respectively. In comparison to the historical mean rates, the DOD rates for 2014 were about the same while the DON rates were lower. In regards to infection burden, due to low case counts, the rates for HO bacteremia, HO UTIs, SSIs, CLABSIs, and VAP were not calculated for either the DOD or DON for the surveillance period.

Table 5. Overall Hospital-Acquired Infection Metrics for Vancomycin-Resistant *Enterococcus* species Infections in the DOD and DON[a]

	DOD		DON	
	2014	Historic[b]	2014	Historic[b]
Exposure Burden	**Overall Rate**	**Mean Rate(95% CI)[c]**	**Overall Rate**	**Mean Rate(95% CI)[c]**
Overall	24.8	24.9 (12.5, 37.3)	22.6	25.0 (16.5, 28.7)
Admission	19.1	19.1 (11.2, 27.0)	16.0	19.7 (10.8, 21.1)

[a]Rates were calculated per 100,000 admissions
[b]Historic mean rates were calculated from the 2005-2013 rates for each parameter.
[c]95% confidence intervals ewre calculated based on Poisson distribution, two-tailed.
Data Source: NMCPHC Health Level 7 (HL7) microbiology and Standard Inpatient Data Record (SIDR) data.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center on 2 June 2014.

Discussion

Since 2005, the overall VRE incidence rate declined. This is true for the DOD beneficiary population in 2014. The DOD annual rate for 2014 was lower than the mean historical rate by 0.1 (6.7%) whereas the DON annual rate was higher than the mean historical rate by 0.3 (15.8%).These increases may be influenced by the use of new data processing software with potential to enhance data capture.

Within the DOD and DON, demographic groups most impacted by VRE infections were people aged 65 or older, retired, Navy sponsors and beneficiaries located in the West TRICARE region. For the DOD, VRE infection rates were higher among males while the DON had higher rates in females. VRE can colonize the genital tract in both females and males, however, females are more prone to UTIs than men, therefore, it is expected that females would be more likely to acquire infection than males.[26] Higher rates of VRE infection are also expected among people aged 65 or older. As a person ages, they are more likely to become ill and end up in the hospital where many of the VRE infections are acquired.[25]

Most VRE infections in 2014 occurred in the outpatient and inpatient setting for the DOD and DON, respectively, and the majority of infections were classified as community onset. Healthcare associated infections represented about a quarter of infections in the DOD and DON. Historically, about 30% of *Enterococcus* health-care associated infections are vancomycin-resistant.[25] Hospital associated VRE infections pose a serious threat on hospitalized patients, especially among patients with prolonged hospital stays. Fortunately, the DOD and DON

healthcare associated cases of VRE decreased by 14.3% and 23.7%, respectively, compared to 2013. A NHSN report showed that the percent of healthcare associated VRE infections decreased from 4.0% in 2006-2007 to 3.0% in 2009-2010.[25,26] Reports for healthcare associated VRE infections in the general population in 2014 are not readily available so a direct comparison to the DOD and DON is not currently possible.

Classifications for healthcare associated VRE infections may overlap with community onset since healthcare associated classifications include patients with disease onset following recent exposures to healthcare delivery within the community. Although there is no community reservoir for VRE in the US, research has shown that patients can remain colonized for weeks or even months and are often still colonized at the time of readmission to the hospital.[8] This leads to potential VRE transmission within the community and healthcare facilities, especially long-term care facilities.

Whether VRE is acquired in the community or the hospital, VRE infections can still be treated with effective antibiotics. Over the surveillance period, daptomycin and linezolid susceptibility remained stable with an average of 100% and 92.9% susceptibility, respectively. Although daptomycin and linezolid maintain the highest susceptibility of all drugs listed, in 2014 daptomycin and linezolid susceptibility decreased by 10.6% and 6.2%. Susceptibility for gentamicin, an antibiotic also recommended for VRE treatment, and streptomycin also decreased in 2014. These declining susceptibilities is very concerning as the availability of effective treatments is extremely important for treating VRE infections and preventing mortality and morbidity.

The admissions prevalence metric measures the magnitude of VRE imported into the healthcare system, and the overall prevalence rate measures the reservoir of infection in a healthcare setting.[22] Current infection control practices in the healthcare setting appears effective, as exposure burden metrics for the DON in 2014 are lower than the calculated historic mean rate. This indicates that fewer people with VRE infections are being admitted to the hospital and that hospitals are decreasing patient's exposure to other patients with VRE. These are excellent methods to limit VRE exposure to high-risk populations such as the elderly, severely ill or long-term care patients. However, in the DOD the calculated exposure burden metrics for 2014 are the same as the historic rates, indicating more admissions and hospital exposures. This could be due to the enhanced data capture in 2014.

Overall, the incidence rates of VRE are fluctuating from year to year in the DOD and DON. No substantial changes in VRE risk groups were seen for 2014 as the infection continues to affect elderly females and manifest as urinary tract infections. The main difference from 2013 to 2014 was observed in antibiotic susceptibility. Although daptomycin, linezolid, gentamicin and streptomycin remain viable treatments for VRE, susceptibilities for all four drugs decreased in the last year. Enforcing antibiotic prescription guidelines must be a priority to ensure the effectiveness of these drugs. Fortunately, healthcare associated infections decreased in 2014, which limits the exposure to patients at risk for VRE, such as the elderly.

Limitations

HL7 data are generated within the Composite Health Care System (CHCS) at fixed MTFs. Microbiology testing results only report the organism(s) that were identified, not what the test was intended for (e.g., if a physician suspects an organism different from the one that was identified, the record will not show the organism that the physician suspected).

Microbiology data are useful for identifying laboratory-confirmed cases of illness. Laboratory-confirmed VRE specimens only indicate that a VRE was isolated, not that it is the primary cause of infection. Dual infections were not analyzed. Cases in which a physician chooses to treat presumptively without laboratory confirmation are not captured. Clinical practice with regards to culturing varies between providers and facilities. Examples of situations where cultures may not be performed include confirmatory tests for patients with influenza-like illness symptoms, or patients with superficial infections who are treated presumptively. Cases in which a physician chose to treat based on a positive surveillance culture are also not captured. Therefore, the isolate counts here are likely an underestimate of the actual VRE burden in the DOD and DON.

The use of microbiology data for analysis of antibiotic resistance is limited by the practice of cascade reporting, where antibiotic sensitivity results are conditionally reported to CHCS to guide treatment decisions. Cascade reporting is practiced to varying degrees at DOD MTFs. Non-standard test records are not be captured in the HL7 restructure process (e.g., when an organism or antibiotic names appear in the test result field). Thus, a complete picture of the susceptibility patterns for VRE isolates is not known, and the presumption of reduced susceptibility is applied to all antibiotics in a class if an isolate is shown to be resistant to that class. It is also important to note that DOD laboratories do not all use the same breakpoints to interpret susceptibility results, thus making MDRO identification subject to some inconsistency.

A SIDR is created at discharge or transfer from an inpatient MTF for all DOD beneficiaries. For active duty personnel, this occurs for non-military medical treatment facility discharges as well. For all other DOD beneficiaries, a SIDR is only created on discharge from a MTF. Patient encounter records depend on correct ICD-9-CM coding practices. Data for medical surveillance are considered provisional and medical case counts may change if the discharge record is edited after the patient is discharged from the MTF.

SIDR data are also limited in that it is difficult to associate a specific microbiology record with a procedure, particularly when a patient has multiple surgeries. If a specimen source was unspecified then the isolate could not be definitively linked to a procedure or device ICD-9-CM code. This potentially makes the SSI rate an overestimate. In addition, if an individual underwent multiple surgeries it was difficult to attribute a positive VRE specimen to a single surgery as the procedure dates do not appear reliably in the data. Also, the values used to calculate the metric density-rate for SSIs and VAP respectively are very small due to low numbers of infections identified in these categories. These results should therefore be considered with caution.

It is possible that not all antibiotic prescriptions were dispensed in response to a VRE infection. Antibiotics that were prescribed within the appropriate timeframe to be associated with a VRE specimen collection date may have been provided for reasons other than the VRE infection, such as a different infection occurring after the VRE species was isolated. However, most antibiotics identified as being associated with a VRE infection were antibiotics that are typically used to treat VRE, and therefore likely that the majority of prescriptions in this analysis were truly in response to VRE infections.

Cases where a physician chose to treat presumptively were not captured as HL7 microbiology records. As only VRE isolates were identified, it is unknown if patients had a concurrent infection with another organism that a prescribed antibiotic could have alternatively been intended for. However, the majority of antibiotics prescribed were antibiotics that could be used in the treatment of a VRE infection, leading one to believe VRE was the intended target for the antibiotic prescription.

All the above mentioned databases are limited in that they do not include data from purchased care, shipboard facilities, battalion aid stations, or in-theater facilities. Therefore, these results are only an estimate of the true VRE infection burden in the DOD and DON. In an effort to account for data lag and capture all finalized records from 2014, data were pulled after a waiting period of four months (data pulled April 2015). The majority of records used in this analysis are presumed with some certainty to be final, but there is the possibility that some records were updated after the data were pooled.

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